**REMARKS**

Consideration of the present application in view of the following remarks is respectfully requested.

**Status of the claims**

Claims 1-26, and 29 are pending.

**Rejection of claim 1 under 35 U.S.C. § 112**

Claim 1 was rejected under 35 U.S.C. § 112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." The Examiner specifically asserted that the claim is indefinite due to the use of the word "sample".

In response, Applicants respectfully submit that the term "sample" is clear as used in claim 1. As the sample size could be any size, it is impossible to limit the claim to a particular size. The specification at page 22 describes the method of measuring bulk density; two grams of the material is poured from weighing paper into a 100 $cm^3$ graduated cylinder. The volume occupied by the powder in the cylinder is measured and the weight determined. The bulk density is calculated as the weight of the powder divided by the bulk volume. Therefore, any amount from the material measured is considered a sample.

**Rejection of claims 1-9 under 35 U.S.C. § 102(b)**

Claims 1-9 were rejected under 35 U.S.C. § 102(b) "as being anticipated by WO 96/32096. The Examiner specifically stated that "WO '096 discloses particles used for drug delivery comprising various amino acids such as leucine . . . diameter is less than 5.2 μm, with particles of less than 5 μm . . . [t]hickness would inherently also be within the claimed

parameters . . . [s]ince diameter and size are also within the claimed parameters, bulk density (a function of mass/volume) would also be inherent."

In response, the Examiner's attention is respectfully directed to claims 1, 3 and 4 which recite as follows:

> 1. *Amino acid particles in which a sample of the particles has a bulk density not more than 0.1 g/cm$^{-3}$.*
>
> 3. *Amino acid particles having a mass median aerodynamic diameter (MMAD) not more than 5$\mu$m.*
>
> 4. *Amino acid particles being in the form of flakes having a thickness of not more than 0.5$\mu$m.*

It is respectfully submitted that the Examiner has failed to fully appreciate that claim 1 recites amino acid particles in which a sample of the amino acid particles has a bulk density of not more than 0.1 g/cubic centimeter. Similarly, claim 3 recites amino acid particles having a mass median aerodynamic diameter (MMAD) not more than 5$\mu$m. Claim 4 also recites amino acid particles being in the form of flakes having a thickness of not more than 0.5$\mu$m.

In contrast, the diameter and particle values relied upon by the Examiner in the '096 publication are not described in the context of an amino acid particle itself, but rather described in the context of a powder composition comprising an excipient (which may include an amino acid e.g., leucine), an active agent and a polypeptide.

Thus, the '096 publication does not, as the Examiner asserts, disclose "amino acid particles having a mass median aerodynamic diameter (MMAD) not more than 5$\mu$m" as recited in claim 3 and the Examiner's rejection is overcome.

In as much as the Examiner's rejection of claims 1, 3 and 4 was based on an incorrect interpretation of the particle sizes disclosed in the '096 publication, the Examiner's rejection of these claims should be withdrawn on this basis alone.

In any event, regarding claim 1, there is absolutely no indication in the '096 publication, that the leucine itself has a bulk density of no more than 0.1 g/cubic centimeter. To the contrary, as described at page 9, lines 14-17 of the '096 publication, the leucine used therein is commercially available leucine. As described in the present application at page at page 5, lines 21 through 25, the bulk density of currently available standard crystalline leucine is in the range of 0.6 to 0.7 g/cubic centimeter, and the bulk density of leucine that has been milled is in the range of 0.3 to 0.4 g/cubic centimeter. As such, it is respectfully submitted that there is no disclosure or suggestion in the '096 publication of amino acid particles in which a sample of the particles has a bulk density not more than 0.1 g/cm-3, as claimed. Accordingly, withdrawal of the Examiner's rejection of claim 1 is respectfully requested. As claims 2, 6, 7, 8 and 9 depend from and incorporate the limitations of claim 1, it is respectfully requested that these rejections be withdrawn as well.

Moreover, Applicants respectfully disagree with the Examiner's contention that "[s]ince diameter and size are also within the claimed parameters, bulk density (a function of mass/volume) would also be inherent." Even if the '096 publication did teach diameter and particle size specific to the amino acid particle itself, which it fails to do, the publication would still fail to teach a bulk density of not more than 0.1 g/cubic centimeter as recited in claim 1 of the present application. Applicants respectfully direct the Examiner's attention to the second aspect of the present application, which discloses amino acid particles with a MMAD and

particle size of less than 5 μm (see specification at page 6, lines 14-17). The specification then reads at page 9, lines 20-24, "[i]t should be understood, however, that the amino acid of the second and third aspects of the invention, for example, might not have the bulk density requires in respect of the first aspect of the invention." Thus, bulk density is not necessarily determined by diameter and particle size.

Regarding claim 4, Applicants also respectfully disagree with the Examiner's contention that "[t]hickness would inherently also be within the claimed parameters . . ." There is absolutely no indication in the '096 publication, that the leucine itself has a thickness of not more than 0.5$\mu$m. To the contrary, as discussed above, the leucine used in the '096 publication is commercially available leucine and, as described in the present application at page 7, lines 15-17, it is respectfully submitted that the thickness of currently available standard crystalline leucine is at least 1 μm and usually greater than 5 μm. As such, it is respectfully submitted that there is no disclosure or suggestion in the '096 publication of amino acid particles that have a thickness of not more than 0.5$\mu$m, as claimed. Accordingly, withdrawal of the Examiner's rejection of claim 4 is respectfully requested. As claim 5 depends from and incorporates the limitations of claim 4, it is respectfully requested that this rejection be withdrawn as well.

Finally, Applicants respectfully disagree with the Examiner's assertion that the WO '096 "uses spray drying with same inlet and outlet temperature parameters" as taught in the examples of the present application and the Examiner's apparent suggestion that this establishes that the particles of the '096 publication are within the claimed ranges of the present application.

The Examiner's attention is respectfully directed to page 19, lines 15-21 of the '096 publication, which reads, "[g]enerally the inlet temperature and the outlet temperature of the spray dry equipment are *not critical* . . . The inlet temperature thus may be between temperatures of 80°C to about 150°C with the outlet temperature being at temperatures of about 50°C to 100°C. Preferably, these temperatures will be from 90°C to 120°C for inlet and from 60°C to 90°C for

outlet." (emphasis added). In contrast, the present application at page 19, lines 3-13 reads, "[i]t is also believed that a high temperature for the spray drying is of importance . . . the inlet temperature of the spray dryer may be *greater than 150°C*, preferably greater than 200°C at ambient temperature. The temperature of spray drying is of *particular importance* for materials which sublime and then condense to form the desired particle morphology." (emphasis added). Applicants note that leucine is a preferred amino acid in the present application as it sublimes. (See specification at page 5, lines 16-21). Applicants point out that spray drying in all the examples of the present application was conducted using the disclosed temperatures.

As the '096 publication teaches a spray drying method which utilizes different temperature than that exemplified in the present application, the Examiner's argument that the process of the '096 publication inherently produces the particles of claims 1, 3, and 4 necessarily fails. On this basis as well, the Examiner's rejection of claims 1, 3 and 4 should be withdrawn.

**Claims 10-23, 25, 26, and 29 Objected to for being Dependent on a Rejected Base Claim**

The Examiner objected to dependent claims 10-23, 25, 26 and 29, asserting that they are dependent upon rejected base claims. As claim 10 has been rewritten in independent format, it is respectfully submitted that this objection be withdrawn. As claims 11-17 depend from and incorporate the limitations of claim 10, it is respectfully submitted that this rejection be withdrawn as well. As claims 18-20 have also been rewritten in independent format, this rejection should be withdrawn. As claims 21, 25, 26 and 29 depend from and incorporate the limitations of claim 19 and claims 22-23 depend from and incorporate the limitations of claim 20, these rejections should also be withdrawn.

## CONCLUSION

In view of the above, it is respectfully requested that the pending objections and rejections be withdrawn. It is believed that all claims are now in condition for allowance.

An early and favorable action on the merits is earnestly solicited.

Respectfully submitted,

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